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10/700,933	11/04/2003	Dale A. Davison	18-595-1-1	5933
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VINCENT L. CARNEY LAW OFFICE			EXAMINER	
P.O. BOX 80836			WALLENHORST, MAUREEN	
LINCOLN, NE 68501-0836			ART UNIT	PAPER NUMBER
			1797	
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			12/28/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/700,933

Applicant(s)

DAVISON ET AL.

Examiner

Maureen M. Wallenhorst

Art Unit

1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-12, 14-16 and 21-26 is/are pending in the application.
- 4a) Of the above claim(s) 14-16 and 21-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-12, 14-16 and 21-26 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 7/7/04, 3/15/04.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

1. Applicant's election with traverse of Group I, claims 1-12 in the reply filed on October 19, 1007 is acknowledged. The traversal is on the ground(s) that the search of Group I would necessarily encompass the search of the claims in Groups II, III and IV. This is not found persuasive because a search of Group II would encompass looking for an apparatus containing pumps, mixers and a controller, which is not required for Group I. A search of Group III would encompass looking for an apparatus containing a central station, a means for sorting gradient tubes and a plurality of remote stations, which is not required for Group I. In addition, a search of Group IV would encompass looking for a shipping container, which is not required for Group I.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

On line 8 of claim 1, the phrase "in a separation of process" does not make proper sense.

Claim 7 is indefinite since the preamble of the claim recites a method of forming a density gradient solution. However, the last step of the method recites forming an immobilized density gradient solution **tube**. Therefore, there is a lack of consistency between the preamble and the last step of the method recited in claim 7.

Claim 9 is indefinite since it recites that the step of re-mobilizing a unit comprises freezing the unit. However, it is understood from the specification that the step of immobilizing the units comprises freezing the units, not the step of re-mobilizing. Rather, the specification indicates that the tubes are warmed in order to remobilize the frozen units.

On line 5 of claim 10, the phrase "the highest density fluid" lacks antecedent basis since line 2 of claim 10 recites a **high** density fluid. In addition, the term "highest" indicates that there are more than two fluids being mixed together.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-2 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Luthe (article from Analytical Biochemistry).

Luthe teaches of a method for the preparation and storage of sucrose gradients. The method comprises placing a first volume of a 40% sucrose solution into a density gradient centrifugation tube, and quickly freezing the solution so as to immobilize it. After the 40% layer is frozen, a 30% sucrose layer is added and frozen. A 20% and 10% sucrose solution is then added to the tube in the same way with freezing after each addition of each layer. By using this method, Luthe teaches that any number of sucrose gradients can be prepared simultaneously, and

stored in the freezer indefinitely for later use. Luthe teaches that when it is desired to use a sucrose density gradient to perform a separation process, such as for the separation and analysis of polyribosomes and RNA, a gradient is removed from the freezer and slowly thawed for 12 hours at 4°C. Therefore, the teaching of Luthe anticipates instant claims 1-2 and 7-9 since the method of Luthe rapidly prepares multiple sucrose gradients by freezing or immobilizing layers of different density materials. The advantages of the method are that many sucrose gradients can be prepared simultaneously and stored at -20°C indefinitely. Gradients can be stored up to 1 year, and if a gradient is removed from the freezer at the end of a day, it will be ready for use the next morning. See pages 230 and 232 of Luthe.

6. Claims 1-2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Radosevich et al (US 4,756,346).

Radosevich et al teach of a method for the preparation of multiple density gradients. The method comprises using a gradient former to form multiple continuous or discontinuous sucrose gradients. A sucrose step gradient composed of equal volumes of 2.5%, 5.5%, 11% and 22% sucrose solution is prepared by the gradient former in a tube. Radosevich et al teach that the sucrose gradients can be immobilized once formed by freezing the tubes in which they are formed. When it is desired to use a density gradient, the tube is taken out of the freezer and thawed and brought to 4°C. Radosevich et al teach that in an 8 hour work day, 48 gradients can be easily made and frozen for use at a later time. This method of using preformed frozen density gradients is used to reduce the work load on busy research days. The method also provides uniform gradients for experiments which require samples to be loaded or run over an extended period of time. Radosevich et al teach that the preformed sucrose gradients can be used to

separate subcellular components of the cellular slime mold *Dictyostelium discoideum*. See 39-55 in column 3, lines 34-68 in column 4 and lines 1-10 in column 5 of Radosevich et al.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 3-4, 6 and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Luthe or Radosevich et al. For a teaching of both Luthe and Radosevich et al, see previous paragraphs in this Office action.

Both Luthe and Radosevich et al fail to teach of combining sucrose solutions of different densities into a series of different proportions, and then layering these solutions in a centrifuge tube. Both Luthe and Radosevich et al also fail to teach of first bringing the different density sucrose solutions close to the freezing point and then layering the almost frozen solutions in a cold gradient tube. Finally, both Luthe and Radosevich et al fail to teach that the frozen sucrose gradients can be packaged and shipped to a different location for use elsewhere.

However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine sucrose solutions of two different densities into a series of different proportions, and then layer the resulting different density solutions into a gradient tube since both Luthe and Radosevich et al teach that in order to form sucrose gradients, sucrose solutions of different densities are layered on top of one another in a gradient tube, and the combination of two different density sucrose solutions in different proportions to one another to form multiple, layered different density solutions achieves the same result as layering different known density sucrose solutions in a gradient tube. It also would have been obvious to one of ordinary skill in the art to first bring the known different density sucrose solutions taught by both Luthe and Radosevich et al close to the freezing point and then layer the almost frozen solutions into a cold gradient tube since such steps achieve the same result as simply freezing the liquid layered, different density sucrose solutions in the tube taught by Luthe and Radosevich et al, and both techniques are recognized as part of the ordinary capabilities of one skilled in the art. It also would have been obvious to one of ordinary skill in the art to package and ship the frozen sucrose density gradients taught by both Luthe and Radosevich et al since both Luthe and Radosevich et al teach that the advantage of such frozen gradients is the ability for a laboratory to have pre-made gradients on hand for use at a later time, and the packaging and shipping of pre-formed materials to other locations/laboratories is part of the ordinary capabilities of one skilled in the art in order to reduce the time and skill required to perform a density gradient separation method. In addition, a person of ordinary skill in the art has good reason to pursue the known options of packaging and shipping laboratory materials within his or her technical grasp using nothing but ordinary skill and common sense.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Please make note of: Shore et al (article) who teach of a method of forming preformed sucrose gradients; Murayama et al (article) who teach of a method for performing density gradient separation using a density gradient prepared by freezing and thawing; and Coombs (US 5,171,539 and 5,266,273), Alexandrov et al (US 4,954,253) and Anderson (US 6,709,871, 6,641,517 and 6,390,966) who all teach of methods and apparatuses for forming solution density gradients.



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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Thursday from 6:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst  
Primary Examiner  
Art Unit 1797

mmw

December 10, 2007

*Maureen M. Wallenhorst*  
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PRIMARY EXAMINER  
GROUP 1700